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PRINCIPAL INVESTIGATOR: Dr. Susan E. Kane

CONTRACTING ORGANIZATION: City of Hope National Medical Center
Duarte, California 91010-3000

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13. ABSTRACT *(Maximum 200 Words)*

The objective of the City of Hope (COH) Breast Cancer Training Program is to develop a new generation of basic and clinical scientists trained to do research on breast cancer and its prevention. The Program will draw predoctoral trainees from the COH Graduate School and postdoctoral trainees from the basic sciences and clinical oncology disciplines at COH. Those who show a genuine interest in breast cancer research, as determined by a written application, are admitted into the Program. The overriding goal of the Breast Cancer Training Program is to provide outstanding training in the basic and translational science of cancer biology, with a special emphasis on breast cancer. Recognizing that cancer is a multi-faceted disease, trainees are required to work in laboratories that study the fundamentals of cancer biology and to develop research projects that focus on the special problem of breast cancer. Specific projects are approved by the Internal Advisory Committee, which includes experts in clinical research and basic science research, and leaders of the COH graduate school and clinical oncology training programs. In addition to completing their standard graduate and postdoctoral education, trainees in the Breast Cancer Training Program take inter-disciplinary coursework in 1) the biology and pathology of breast cancer; 2) breast cancer prevention and treatment; 3) the ethical conduct of basic and clinical research; 4) statistics as it relates to biological and cancer problems; 5) genetic pre-disposition to breast cancer and genetic counseling; and 6) quality of life/pain management of breast cancer patients. Trainees participate in seminars to share the results of their research and to review contemporary research literature in breast cancer; they attend lectures presented by speakers from outside of COH who are experts in the field of breast cancer; and they take advantage of a variety of seminars at COH having to do with other areas of basic science and translational research.

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PROGRESS REPORT

Title: Training Program in Breast Cancer Research
Number: DAMD17-00-1-0203
Principal Investigator: Susan E. Kane, Ph.D.

Key Accomplishments:

- Admitted 5 trainees (3 graduate students, 2 research fellows) into the 2000-01 class and 3 additional trainees (1 graduate student, 1 research fellow, 1 clinical fellow) into the 2001-02 class.
- In the 2000-01 academic year, conducted formal courses in "Breast Cancer Biology and Pathology" and "Biostatistics and Bioinformatics" and initiated formal interactions (Journal Club, symposia, web discussions) with the new training program in Clinical Cancer Genetics.
- Held bi-weekly meetings with all trainees and mentors alternating between Journal Club and Data Exchange formats, all centered on breast cancer research.
- Supported high-quality research related to breast cancer biology (see summary of trainee activities below). Support for one trainee led to his successful application for an individual predoctoral fellowship from the DOD.
- Sponsored or co-sponsored guest lectureships/seminars by prominent breast cancer researchers, including Dr. Susan Horwitz (Albert Einstein College of Medicine), Dr. Ellis Levin (UC Irvine), Dr. Jamil Momand (California State University, Los Angeles), Dr. Anna Wu (University of Southern California).
- Supported travel for 2 trainees to present their work at national meetings.
- Recruited 2 additional faculty members as mentors -- Dr. Ren-Jang Lin (Professor of Molecular Biology) and Dr. Benjamin Paz (Surgeon and Director of COH's Breast Cancer Clinic)

Progress with respect to Statement of Work:

Task 1. Recruit trainees into the Breast Cancer Training Program. All items within this Task have been accomplished except for the development of advertising material to recruit new trainees, including minorities, to City of Hope (COH). Recruitment so far has taken place in the context of existing students and fellows at COH, although we have worked with the graduate school and fellowship programs to include the Breast Cancer Training Program as part of their recruitment efforts (during interviews and screening of candidates). This latter aspect of recruitment was listed as a goal within this Task (Work with the Graduate School and Surgical Oncology Fellowship Program to recruit qualified candidates who express an interest in breast cancer research). In fact, we admitted a trainee from the Surgical Oncology Fellowship Program into our 2001-02 class of trainees.

Task 2. Assign trainees to laboratories and identify breast cancer-related projects. This has been accomplished for the 2000-01 and 2001-02 classes of trainees.

Task 3. Initiate required coursework, journal clubs, and data exchange forums. Three of the courses in our stated curriculum have been initiated (see attached curriculum in Appendix). A fourth course is in the form of ongoing "grand rounds" and it includes Breast Cancer trainees as appropriate to the topic area. A fifth course is still in development. The Journal Club and Data Exchange forums have been established in the form of a bi-weekly meeting with trainees and mentors. All 5 trainees

presented at least twice during the 2000-01 academic year and several mentors presented journal clubs as well (see attached schedule in Appendix).

Task 4. Monitor progress of past and current trainees and quality of the Program. Progress of graduate student trainees is monitored in the context of their required advisory committee meetings, which meet every 6-12 months for each trainee. Written progress reports were also received from all trainees as a requirement for their continuation in the program. At the same time, we solicited feedback from the trainees on their suggestions for improving the program and we will take those suggestions into consideration in the coming years. The Internal Advisory Committee has met 3 times as an entire body and we have conducted frequent e-mail correspondence. The initial meeting was to establish the parameters of the program and assign responsibilities for coursework. Subsequent meetings and correspondence have been to keep track of trainees' progress, review applicants for open trainee slots, and discuss improvements to the program (see minutes of meetings in the Appendix).

Task 5. Establish a Distinguished Speaker series with experts in the field of breast cancer research. We have not established a formal series but we have sponsored or co-sponsored several guest speakers. Meetings with our trainees are specifically arranged during the time these guests are on campus and trainees are required to attend the seminars. This year, we will proceed with our plans to establish a committee of trainees and faculty to invite appropriate speakers on behalf of the Program. In addition, we have suggested that an upcoming Beckman Symposium (an annual event attended by COH and other community scientists) be centered on gender-related cancers. The Program would participate in the organizing of such a symposium.

Specific trainee progress/Reportable outcomes:

Following are excerpts from trainee progress reports and a list of their specific accomplishments during the 2000-01 academic year.

Carmel Chan (graduate student; Susan Kane, mentor): The Her2 oncogene encodes a 185 kDa type I tyrosine kinase receptor that is highly homologous to the epidermal growth factor receptor (EGFR). Her2 is overexpressed in 25-30% of human breast cancers and its overexpression is associated with poor prognosis and response to chemotherapy. Herceptin is a recombinant, humanized antibody directed against Her2 and it has been shown to inhibit the *in vitro* and *in vivo* proliferation of breast cancer cell lines that overexpress Her2. Herceptin is currently approved for use in Her2-positive breast cancer patients but only about 25% of these breast cancers respond to Herceptin. The purpose of our work has been to investigate the mechanism by which breast cancer cells are resistant to Herceptin. We have selected and subcloned BT474 human breast carcinoma cells that are 400- to 4000-fold resistant to Herceptin. We have characterized the expression of Her2 -- cell-surface, total cellular, and phosphorylated forms -- as well as expression of related receptors EGFR, Her3 and Her4 in the resistant cells. We found that levels of cell-surface, total and phosphorylated Her2 remained high in the Herceptin-resistant cells, even in the continuous presence of 0.2 μM or 1.0 μM Herceptin. These same concentrations of Herceptin are sufficient to cause down-regulation of total Her2 and complete abolishment of phosphorylated Her2. We are currently investigating the mechanism of maintained Her2 phosphorylation and the significance of this observation to the resistant phenotype.

Manuscript:
Chan, C.T. and Kane, S.E. (2001) *In vitro* selection and characterization of Herceptin-Resistant Breast Cancer Cells. Submitted.

Abstracts:

Chan, C.T. and Kane, S.E. *In vitro* selection and preliminary characterization of Herceptin Resistant Human Breast Carcinoma Cells. 92nd Annual Meeting of the American Association for Cancer Research, 2001.

Chan, C.T. and Kane, S.E. Characterization of Her-2 levels and half-lives of cell-surface Herceptin®/Her-2 complex in Herceptin resistant human breast carcinoma cells. AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, 2001.

Presentations:

RSO Lake Arrowhead Advance, Beckman Research Institute, 2001

Advanced Topics in Biology, Cal Poly Pomona, 2001

Development of cell lines:

16 Herceptin-resistant BT474 human breast cancer cell lines (BT/HerR 0.2 A- J and BT/HerR 1.0 A-F)

Funding received and applied for:

Carmel Chan: "*In vitro* selection and characterization of Herceptin-resistant human breast carcinoma cells" US Army Predoctoral Fellowship Award in Breast Cancer Research (received).

Susan Kane: "Analysis of BT/Her^R cells selected for resistance to Herceptin" National Cancer Institute (submitted).

Dawn Ratay (graduate student; Adam Bailis, mentor): Dawn's project has to do with the effects of expressing human *BRCA*1 on recombination in yeast. After constructing a plasmid for the constitutive expression of human *BRCA*1 in yeast, Dawn tested whether the plasmid had an impact on the insertion of short DNA sequences into the yeast genome. This assay was chosen because these events are known to require the Mre11/Rad50/Xrs complex with which Brca1 protein is known to be associated in human cells. While no significant effect on short-sequence recombination was observed in the cells containing the *BRCA*1 plasmid, Dawn did notice an effect on gene conversion in the assay strains. She followed up on this observation with a second assay that measures the frequency of gene conversion between unlinked repetitive sequences. She found that the frequency of gene conversion was 5- to 8-fold lower in the strain containing the *BRCA*1 plasmid than in a strain containing an empty plasmid. This suggests that Brca1 protein might interfere with normal recombination, perhaps by binding to its normal DNA substrate(s) and blocking endogenous yeast recombination factors. In the second year of the fellowship, Dawn will continue this work in several ways. First, she will confirm expression of the *BRCA*1 cDNA in yeast by Western blot analysis. Second, she will repeat the gene conversion assays in isogenic yeast strains containing mutations in single DNA repair and recombination genes in an effort to determine which recombination factors Brca1 might be blocking. In this manner, Dawn will work towards determining the action of Brca1 in yeast at the DNA level, and ultimately, its role in human DNA repair.

Abstract:

RSO Lake Arrowhead Advance, Beckman Research Institute, 2001

Julia Kirshner (graduate student; Jack Shively, mentor): A model of mammary morphogenesis involves growth of mammary epithelial cells in a three-dimensional culture of Matrigel (a source of extracellular matrix). The resulting acini include lumens that are thought to be formed by apoptosis of the cells within the center of the spherical colonies. Recent studies have shown that biliary glycoprotein (CEACAM1), which is a cell-cell adhesion molecule that is expressed on the lumenal surface of most epithelial cells, may be involved in lumen formation. The goals of this project are to determine the specific roles of CEACAM1-L and CEACAM1-S in lumen formation and to determine the apoptosis signal transduction pathway that CEACAM1 employs. To address the first question,

both the long (CEACAM1-L) and short (CEACAM1-S) versions of CEACAM1 were transfected into MCF7 cells, which normally lack CEACAM1 and do not form lumens in Matrigel. Transfection of CEACAM1-S led to lumen formation but transfection with CEACAM1-L led to cell death. In CEACAM1-S transfected cells, lumen formation occurred over a 12-day timeframe, with 10% lumen formation at 3 days, 17% at 5 days, 23% at 7 days, 41% at 9 days and 61% at 12 days (similar to the time course of lumen-positive MCF10A cells. All evidence to date points to CEACAM1-S either directly or indirectly causing apoptosis in the cells that fill the lumenal space, allowing for the true lumen to be formed. Current studies are aimed at understanding the role of serine and threonine phosphorylations on lumen formation and apoptosis. Preliminary indications suggest that phosphorylation at a critical serine may prevent apoptosis and lumen formation. Studies are also underway to determine the apoptotic pathway employed by CEACAM1 in this system.

Abstracts:

Kirshner, J., Chen, C., Schumann, D., Liu, P., Huang, J., and Shively, J. Induction of lumen formation in MCF7 mammary carcinoma cells transfected with CEACAM1-S and grown in Matrigel. Poster presentation at CEA Symposium

Kirshner, J., Chen, C., Liu, P., Huang, J., and Shively, J. Role of apoptosis in mammary morphogenesis model system. Poster presentation at RSO Lake Arrowhead Advance.

Manuscript in preparation:

Kirshner, J., Chen, C., Liu, P., Huang, J., and Shively, J. Phosphorylation of CEACAM1-S induces lumen formation and apoptosis in transfected MCF-7 mammary carcinoma cells.

Toru Itoh, Ph.D. (research fellow; mentor, Shiuan Chen): Dr. Itoh's research effort has been focused on the molecular characterization of Snail and Slug in human breast cancer cells, using the aromatase promoter I.3 as the target. Snail is a DNA binding protein that binds to a region in the human aromatase gene that is overlapping with CREaro, a cAMP responsive element. Mammalian transient transfection experiments have revealed that Snail acts as a repressor on aromatase promoter I.3. Dr. Itoh performed site-directed mutagenesis experiments that demonstrated that the N-terminal 20 amino acids (SNAG domain) play important roles in the repressor activity of Snail. Semi-quantitative RT-PCR analysis on the stably Snail-transfected MDA0MB-231 cell lines demonstrated that over-expression of Snail down-regulates aromatase expression. Slug is another DNA binding protein that binds to the CREaro region in the human aromatase gene. DNA competition experiments using mutant competitors have revealed that Slug protein binds to CREaro rather than SnaH-binding site. Mammalian transfection experiments demonstrated that Slug acts as a repressor on aromatase promoter I.3 in HepG2 cells, but does not have any effects in MCF7 or SK-BR-3 breast cancer cells. Dr. Itoh's RT-PCR analysis on Snail, Slug, and CREB led to the hypothesis that the different responses of each cell line to Slug may be due to the various intracellular expression levels of Snail, Slug and/or CREB proteins. Current efforts are focused on establishing stably transfected MCF7 cells that express Snail, using a Tet-inducible expression system. Dr. Itoh is also planning to perform co-transfections with Snail, Slug and CREB to determine how these proteins compete with each other at the functional level. During this project, the investigators have gained a better understanding of the differences in function of Snail and Slug in breast cancer cells through the molecular characterization of these proteins that interact with the CREaro region in the human aromatase gene.

Abstract:

Okubo, T., Truong, T.K., Yu, B., Zhao, J., Itoh, T. and Chen, S. Down-regulation of promoter I.3 activity of the human aromatase gene in breast tissue by zinc-finger protein, Snail (SnaH). 92nd Annual Meeting of the American Association for Cancer Research, 2001.

Hye-Dong Yoo, Ph.D. (research fellow; Barry Forman, mentor): Dr. Yoo's project is focused on finding the endogenous ligand for an orphan nuclear receptor, the Steroid and Xenobiotic Receptor (SXR). SXR is a master regulator that controls the expression of several genes including CYP3A4, CYP2C9, and *MDR*1, genes that are involved in metabolism, clearance and resistance to a variety of chemotherapeutic agents. Several compounds are known to be capable of activating SXR in model systems, including paclitaxel, rifampicin, and many steroids, but the endogenous ligand for SXR is not known. Since SXR is expressed mainly in the liver, a liver extract from cow was prepared and tested to see if there might be some components that could activate SXR. Liver extracts were first extracted with water or $CHCl_3$ (organic) and these extracts were used in a luciferase reporter assay for SXR activity. The organic extract had activity in this assay but the water extract did not. Subsequent multi-step fractionation of the organic extract has led to the determination of several active peaks on a final reverse-phase HPLC with 92% MeOH in water. Current efforts are focused on identifying these peaks using appropriate state-of-the-art physical methods available at City of Hope. Dr. Yoo will also explore structure activity relationships to maximize the molecule's potential application. If needed, total synthesis of a desired compound can be completed by collaboration. Finally, the identification of an endogenous SXR ligand will make it possible to compare levels of this compound with paclitaxel responsiveness in breast cancer patients. This could help identify those patients who are most likely to respond to paclitaxel.

Conclusion:

We have accomplished most of goals for the Training Program in Breast Cancer Research at City of Hope. With 5 trainees in the first year and 3 additional trainees in the second year, we have exceeded our expectations in the original training grant application. The applicant pool has been excellent (10 the first year; 11 the second year). All of these trainees are working on breast cancer-related projects (the 3 new trainees have not been detailed here) and all are attending a variety of breast cancer-related courses, seminars, journal clubs, and data sessions. We have had outstanding participation by the faculty mentors of these trainees as well. After one year, it might be too much to expect a high level of reportable outcomes in the way of publications and presentations, but we expect this to change by the end of year 2. Also in year 2, we will strive to expand our seminar speaker series and complete the list of courses offered to all trainees.

APPENDIX 1

Breast Cancer Biology -- 2000

9/6	Basic anatomy, physiology and pathology of breast cancer	Sharon Wilczynski
9/13	Metabolism of the breast cancer cells	Tom Balon
9/20	Tumor suppressor genes and oncogenes	Jamil Momand
9/27	Molecular alteration in breast cancer	Gerd Pfeifer
10/4	Growth factors and signal transduction	Rama Natarajan
10/11	Hormones and breast cancer	Shiuan Chen
10/18	Tumor Angiogenesis	Chu-Chih Shih
10/25	Cell-cell and cell-matrix interaction, metastasis	Jack Shively
11/1	Apoptosis and the development of breast cancer	Warren Chow
11/8	Environmental risk factors	Anna Wu (USC)

Other information

1. There are ten lectures. We meet once a week (5:30 pm to 7:30 pm, Wednesday) at the Conference room in the Miller building.

2. The students will be provided with the slide printout and an outline of the lecture.

3. We will have a textbook that will provide some basic information to the students.

4. Each instructor will provide a question. The students are required to choose a question and write a 5-page term paper which is due on November 22.

5. Contact Shiuan Chen (x2601) if you have any questions.

Breast Cancer Biology -- 2001

9/12	Basic anatomy, physiology and pathology of breast cancer	Sharon Wilczynski
9/19	Growth factors and signal transduction	Rama Natarajan
9/26	Apoptosis – molecular mechanism	Jiing-Kuan Yee
10/3	Tumor suppressor genes	Gerd Pfeifer
10/10	Apoptosis, Survival and Response to Therapy	Susan Kane
10/17	Hormone and breast cancer	Shiuan Chen
10/24	Tumor Angiogenesis	Chu-Chih Shih
10/31	Cell-cell and cell-matrix interaction, metastasis	Jack Shively
11/7	Mammary expression of xenobiotic metabolizing enzymes	Tim Synold
11/14	Breast cancer treatment	Baiba Grube (John Wayne Cancer Inst.)

Other information

1. There are ten lectures. We meet once a week (5:30 pm to 7:30 pm, Wednesday) at the Conference room in the Miller building.
2. The students will be provided with the slide printout and an outline of the lecture.
3. We will have a textbook that will provide some basic information to the students.
4. Each instructor will provide a question. The students are required to choose a question and write a 5-page term paper which is due on November 28.
5. Contact Shiuan Chen (x62601) if you have any questions.

Biostatistics & Biomedical Informatics

Instructors:

Jeffrey Longmate	2478
David Ikle	4446
Yate-Ching Yuan	2161
Paul Frankel	5265
Doug Stahl	5653

Textbooks:

FUNDAMENTALS OF BIOSTATISTICS, 5th edition, Bernard Rosner, Duxbury, 2000.
BIOINFORMATICS : A PRACTICAL GUIDE TO THE ANALYSIS OF GENES AND PROTEINS, Andreas Baxevanis (Ed.), John Wiley & Sons

Grading:

Regular (about weekly) exercises to be handed in. You may work cooperatively, but hand in individual work. There will be no "exams."

Meetings:

Tuesdays and Thursdays at 9:30am, Fox North Conference Room

Every Wednesday at 12:00N
Kaplan Clinical Research Conf. Rm.

CITY OF HOPE
MEDICAL ONCOLOGY AND HEMATOLOGY FELLOWS
LECTURE SERIES
2000-2001

DATE	TITLE	SPEAKER
September 13, 2000	Chemotherapy of Brain Tumors	Morgan
September 20	HLA Tissue Typing	Senitzer
September 27	Journal Club	Lam
October 4	T-Cell Therapy in Lymphoma	Jensen
October 11	Renal Cancer	Margolin
October 18	Prostate Cancer	Twardowski
October 25	Journal Club	Srivasta
November 1	Pituitary Tumors	Kandeel
November 8	Anti-Tumor Antibiotics	Doroshow
November 15*	Regional Perfusion Therapy	Leong
November 22*	Ovarian Cancer	Morgan
November 29	Cervical Cancer Screening	Wilczynski
December 6	Alkylating Agents	Newman
December 13	Hormonal Therapy of Breast Cancer	Reddy
December 20	NO LECTURE	
December 27	NO LECTURE	
January 3, 2001	Journal Club	Lopez
January 10	HIV Update	Ito
January 17	Palliative Care-Use of Novel Meds	Roxby
January 24	Endometrial Cancer	Lin
January 31*	Chemoembolization	Marx
February 7*	Hepatic Resection	Wagman
February 14	Journal Club	Jancis
February 21	Apps of Gene Transfer	Chen
February 28	Stereotactic Radiosurgery	Pagnini
March 7	Cortical Mapping	Mamelak
March 14	Hemorrhagic Cystitis	Wilson
March 21	BMT Topic	Lopez
March 28	Journal Club	Reddy
April 4	Sentinal Nodes in Breast Cancer	Chu
April 11	Applied Pharmacokinetics	Synold
April 18	Cutaneous T-Cell Lymphoma	Molina
April 25	Therapy of Sickle Cell Anemia	Roxby
May 2	BMT/Thalidomide in Myeloma	Somlo
May 9	Journal Club	Al-Kadhimi
May 16	NO LECTURE – ASCO	
May 23*	Hereditary Cancers I-Focus on Colon	Weitzel
May 30	Hereditary Cancers II-Focus on Colon	Weitzel
June 6*	Hodgkin's Disease	Fung
June 13*	Hemolytic Anemias	Tanaka
June 20	Journal Club	Roxby

APPENDIX 2

BREAST CANCER JOURNAL/DATA CLUB SCHEDULE -- 2000

October 2	Journal Club	Susan Kane
October 16	Special Seminar	Susan Horwitz (4:00)
October 30	Data Club	Carmel Chan
November 13	Special Seminar	Chung Lee (4:00)
November 27	Data Club	Toru Itoh
December 11	Journal Club	Julia Kirshner
January 8	Data Club	Hye-Dong Yoo
January 22	Journal Club	Carmel Chan
February 5	Data Club	Julia Kirshner
February 19	Journal Club	Toru Itoh
March 5	Data Club	Dawn Ratay
March 19	Journal Club	Shiuan Chen
April 2	Data Club	Zaid Al-Kadhimi
April 16	Journal Club	Dawn Ratay
May 7	Data Club	Carmel Chan
May 21	Journal Club	Jack Shively
June 4	Data Club	Toru Itoh
June 18	Journal Club	Hye-Dong Yoo
July 2	Data Club	Julia Kirshner
July 16	Data Club	Hye-Dong Yoo
July 30	Data Club	Dawn Ratay
August 13	Data Club	Zaid Al-Kadhimi

APPENDIX 3

Breast Cancer Training Program

Internal Advisory Committee

Minutes for February 23, 2000

Present: S. Chen, J. Doroshow, M. Grant, S. Kane, J. Longmate, S. Novak, J. Rossi, J. Singer-Sam, A. Wu

The meeting was convened by S. Kane at 4:00pm.

1. S. Kane gave an overview of the proposed Program and then initiated discussion about implementation and possible modifications.

2. It was agreed that in addition to the funded positions for students and postdoctoral fellows, the Program should be opened up to other students and fellows who want to participate (but who are funded by other mechanisms). This could include students/postdocs who may want to take one or more of the courses offered by the Program, students/postdocs who may want to participate in the Journal Club or data exchange forum, or clinical fellows who want to focus on breast cancer research as part of their fellowship training. Where applicable, participation as full members of the Program will need to be assured by the research mentor or Director of the fellowship program.

3. It was agreed that, at least for the first year of the grant, applications will be solicited from all interested graduate students (regardless of their seniority in the graduate school) and the best applicants will be supported by the grant. Applicants must coordinate with their research mentor to come up with an appropriate breast cancer-related project, which must be approved by the Advisory Committee. For students completing their first year in graduate school, a list of possible mentors and projects will be generated so that those students wanting to be in the Program can make an informed decision regarding a prospective mentor. S. Kane will put together an announcement to solicit project ideas from mentors who are interested/willing to have students in the Program. It was agreed that this should be open to any faculty member in the graduate school who might have a research project relevant to breast cancer. S. Kane will make a presentation at the RSO Advance regarding the application process and the requirements of participation in the Program.

4. It was agreed that, at least for the first year, applications for postdoctoral fellows will be taken from fellows already working in laboratories doing breast cancer-related research.

5. The application deadline for students and postdocs will be August 1. S. Kane will put together an application form, which will include a brief description of the research project, a statement of intent to participate in all aspects of the Program, and a copy of the applicant's graduate school transcript (if applicable); it may include letters of recommendation. Applications will be reviewed by the Advisory Committee and the best applicants will be admitted into the Program.

6. Curriculum. The 5 course outlines were briefly reviewed and a tentative schedule of courses was proposed: a) *Cancer Biology* will be taught every year beginning in the Fall of 2000. S. Chen agreed to take over as organizer of this course. It was suggested that some of our Seminar budget might be used to bring guest lecturers in to teach parts of this course. b) *Breast Cancer Prevention and Treatment-Responsible Conduct in Research* will be taught every 2-3 years as a

subset of a similar course offered through the K-12 training grant. The next course will begin in the Fall of 2001. The course organizer is Lucille Leong. In addition, trainees will be invited and encouraged to attend weekly the New Patient conference that meets on Thursdays at 8-9:30am in Needleman I. c) *The Genetics of Breast Cancer Risk Assessment* will be given in conjunction with a Clinical Cancer Genetics Fellowship Program being developed by Jeffrey Weitzel. Coordination and timing of the course will be worked out with him. d) *Biostatistics and Bioinformatics* will be taught every other year beginning in the Spring of 2001. This will be a new course developed for the graduate school and perhaps incorporated as a required course into that curriculum. Jeffrey Longmate and Doug Stahl will coordinate the course. e) *Breast Cancer and Quality of Life* will be conducted in a "grand rounds" format on an ongoing basis, meeting once every 1-2 months and covering a range of topics related to quality of life issues in breast cancer patients. In addition, students will be encouraged to participate in patient support groups as a way to make contact with breast cancer patients. Marcia Grant will coordinate this course.

7. Once the Program is underway, a Breast Cancer Journal Club (frequency and format to be determined) and a Data Exchange Forum (monthly) will be established. S. Kane will take responsibility for this.

8. It was agreed that Queenie Du in the Office of Professional Education would provide administrative/secretarial assistance for the Program. Partial support may be available from the grant if the requested budget is awarded.

9. On the question of regulatory compliance, it was suggested that blanket approvals be obtained from the IRB, IBC, and RACC so that official notices of compliance can go to the Army. S. Kane will look into this.

10. Other items on the agenda were deferred to future meetings. These include a) advertising and recruiting prospective trainees to City of Hope and b) establishing a Seminar Series of distinguished speakers in the field of breast cancer research and treatment.

11. It was agreed that future business will be conducted by e-mail as much as possible. A meeting in August will be needed to review applications for the first-year trainees.

Meeting was adjourned at 5:00pm.

Breast Cancer Training Program

Internal Advisory Committee

Minutes for August 9, 2000

Present: S. Chen, S. Kane, J. Longmate, S. Novak, J. Rossi, A. Wu

The meeting was convened by S. Kane at 4:00pm.

1. There was a discussion of the review process and how to rank candidates. We agreed to use an NIH-format scoring system. Each committee member scored each application (unless they were in conflict) and scores were totaled and averaged at the end.

2. We had 10 applications all together, with funding designated for 2 graduate students and 2 postdoctoral fellows. Results of the scoring were such that 1 graduate student (Carmel Chan) was superior and 2 others were highly competitive. After some discussion, it was agreed that Carmel would receive full stipend support and the other 2 (Dawn Ratay and Julia Kirshner) would each receive 50% stipend support. Two postdoctoral fellows (Hye-Dong Yoo and Toru Itoh) were selected as trainees, to receive support up to the level funded by the training grant ($27,700 each).

3. There was a review of the planned course in "Breast Cancer Biology" to be organized by Shiuan Chen and to begin in September and the planned Journal Club/Data Exchange forum to begin sometime in October.

4. There was a discussion of a guest speaker (Dr. Susan Horwitz) and co-sponsorship of her visit by the Breast Cancer Training Program and the Clinical Cancer Center.

Meeting was adjourned at 5:00pm.

Breast Cancer Training Program

Internal Advisory Committee

Minutes for August 2, 2001

Present: S. Chen, S. Kane, J. Longmate, S. Novak, J. Rossi, L. Wagman, A. Wu

The meeting was convened by S. Kane at 4:00pm.

1. S. Kane reviewed the status of the continuing trainees and the financial situation with respect to trainee slots available. Since Carmel Chan applied for and received an individual predoctoral award from the Army, it was agreed that he would continue in the training program but that his stipend would come from his own training grant. In addition, based on her exemplary work as a trainee, Julia Kirshner's support was increased to full stipend (from 50%). Dawn Ratay will stay at 50% support.

2. There was a discussion of the review process and how to rank candidates. We agreed to use a slightly different system this year that would involve numerical ranking of each candidate (1-11, with 1 being the best), a summing and averaging of the ranks, and discussion of candidates with the lowest rank numbers. Each committee member ranked each application (unless they were in conflict) and scores were totaled and averaged at the end.

3. We had 11 applications all together, with funding designated for 1-2 graduate students and 1-2 postdoctoral fellows. Results of the scoring were such that 1 graduate student (Chunxia Li), 1 postdoctoral research fellow (Tove Olafsen) and 1 postdoctoral clinical fellow (Carey Cullinane) were all superior. It was agreed that Chunxia would receive full stipend support (up to the $21,600 designated by the training grant) and the other 2 would receive support up to the level funded by the training grant ($28,000 each).

5. There was a review of the coursework, including "Breast Cancer Biology" and "Biostatistics and Bioinformatics" both of which were conducted last year and will be conducted again this year. We discussed several options for assessing the work of the postdoctoral researchers, in particular, since they do not take these courses for any official credit. We will consider a requirement for an oral presentation in the Breast Cancer Biology course. Assessment and class participation was also an issue in the Biostatistics course.

6. It was agreed that we would be more aggressive about finding out about, dissemination information about, and encouraging trainee attendance at breast cancer-related events on campus and elsewhere. S. Kane will find out the correct contact people on campus, get on appropriate mailing and e-mail lists to receive information in a timely fashion, and make regular checks of websites where this kind of information can be found.

7. There was a discussion of the seminar series. The Program will pay the honorarium for Dr. Ellis Levin in September and will solicit names for other people to invite. We will also recommend a Beckman Symposium topic on gender-related cancers and be part of the organizing effort for this event.

Meeting was adjourned at 5:00pm.